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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,424	04/11/2001	Carlo M. Croce	8666-009	9552

7590 08/29/2003

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/832,424	CROCE ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-9,13,15,17,19 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-9,13,15,17,19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1, 10-12, 14, 16, 18, 20 and 22 have been canceled. Claims 2, 3, 5-9, 13, 15, 17, 19 and 21 are pending and under consideration in the instant office action.

Applicant's arguments filed 6-20-03 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 2, 3, 5-9, 13, 15, 17, 19 and 21 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose genome comprises a heterozygous disruption in FHIT, wherein said disruption causes increased induction of tumor formation, does not reasonably provide enablement for transgenic mice with a homozygous disruption in FHIT, for disrupting any FHIT gene in a mouse or for comparing the mice as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims require the a transgenic mouse having a disruption in an FHIT gene that displays increased susceptibility to visceral or sebaceous tumor formation or increased susceptibility to tumor formation upon being exposed to NMBA relative to FHIT +/+ mice. The purpose of the transgenic taught in the specification is to obtain a tumor model for Muir-Torre Syndrome (MTS) which is characterized by a predisposition for developing a combination of sebaceous and visceral tumors (pg 2, line 5). The specification only teaches FHIT +/- mice having

increased susceptibility to visceral and sebaceous tumor formation or increased tumor formation upon being exposed to NMBA as compared to FHIT +/+.

Applicants argue pg 44, lines 8-32, taught how to make the homozygotes and that the phenotype of the homozygotes is similar to that of heterozygotes. Applicants' argument is not persuasive. The unpredictability in the art regarding the genotype causing the desired phenotype was established in the previous office action. While the specification teaches obtaining FHIT -/- mice that do not express FHIT (pg 44, line 27), the specification does not teach the phenotype of the mice. While the specification teaches FHIT +/- mice have increased susceptibility to tumors, the specification does not compare FHIT +/- to FHIT -/- mice. Without such guidance the specification does not provide adequate guidance for one of skill in the art to overcome the unpredictability in the art to be able to determine how to use FHIT -/- mice or to predict the phenotype of the FHIT -/- mice. Pg 50, lines 24-26, states both FHIT +/- and FHIT -/- are "sensitive to carcinogen" and "will serve as useful models for carcinogen-induction of tumors of various organs," the specification does not teach homozygotes have increased susceptibility to visceral and sebaceous tumor formation or increased tumor formation upon being exposed to NMBA as compared to FHIT +/+ as claimed.

The comparison step in the method claims does not enable one of skill to determine which molecules are carcinogenic. The increased rate of tumor formation following administration of the test molecule must be compared to an animal that did not receive the test molecule to determine that the molecule is carcinogen. The comparison is essential to determining carcinogens and should be included in the claims. Applicants' arguments have been considered, but the claims do not require that increased susceptibility be found in the transgenics rather than the control.

The claims as newly amended encompass disrupting any FHIT gene. The art only taught one FHIT gene. The spec does not teach any other FHIT gene. It would require one of skill undue experimentation to determine other FHIT genes. If other FHIT genes exist, it would have been unpredictable whether such mice would have the phenotype claimed given the unpredictable state of the art regarding the phenotype of transgenic mice. Therefore, the specification does not enable disrupting any FHIT gene as broadly claimed.

Claims 2-9, 13, 15, 17, 19 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"An exon 5 coding region" (claims 2 and 3) does not make sense. There is only ever one exon 5 in a gene; therefore, the phrase should be "the exon 5 coding region." Applicants argue the claim has been amended, but it has not.

The phrase "wherein an increased rate of tumor formation following administration of the test molecule is indicative" (claim 13) is incomplete because it lacks the essential element of comparing to a control. The increased rate can only be determined when compared to a control that did not receive the test compound. Applicants argue the claims do have a comparison step. Applicants' argument is noted; however, the claim does not clearly set forth that the increased rate of tumor formation is in the mouse of claims 2, 5, 6 or 7 as compared to the control mouse. As written, the increased rate of tumor formation may be in the control as compared to the mouse of claims 2, 5, 6 or 7, which does not make sense.

The phrase "wherein a reduced rate of tumor formation following administration of the test molecule is indicative" (claim 15) is incomplete because it lacks the essential element of

comparing to a control. The reduced rate can only be determined when compared to a control that did not receive the test compound. Applicants argue the claims do have a comparison step. Applicants' argument is noted; however, the claim does not clearly set forth that the reduced rate of tumor formation is in the mouse of claims 2, 5, 6 or 7 as compared to the control mouse. As written, the reduced rate of tumor formation may be in the control as compared to the mouse of claims 2, 5, 6 or 7, which does not make sense.

Claim 5 is indefinite because parent claim 2 requires the genome of the mouse has the disruption. If the genome has the disruption, the germline and somatic cells of the mouse must have the disruption. Therefore, claim 5 does not further limit claim 2.

Claims 2, 3, 5-9, 13, 15, 17, 19 and 21 are free of the prior art because the prior art did not teach or suggest transgenic mice having a disruption in an FHIT gene having increased susceptibility to visceral or sebaceous tumor formation or to tumor formation upon being exposed to NMBA.

Conclusion

The following prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Huebner et al. (Annu. Rev. Genet. 1998. Vol. 32, pg 7-31).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

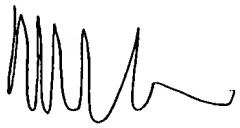
Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER